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*** YOU HAVE NEW MAIL ***

=> s label? (4a) oligonucleotide
L1       29409 LABEL? (4A) OLIGONUCLEOTIDE

=> s l1 and oligonucleotide (3a) solid support
L2         810 L1 AND OLIGONUCLEOTIDE (3A) SOLID SUPPORT

=> s l2 and oligonucleotide(4a) protecting group
L3          42 L2 AND OLIGONUCLEOTIDE(4A) PROTECTING GROUP

=> s l3 and label? (3a) compound
L4           6 L3 AND LABEL? (3A) COMPOUND

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            6 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 bib abs 1-6

L5   ANSWER 1 OF 6  USPATFULL on STN
AN     2008:5056  USPATFULL
TI     System for delivering therapeutic agents into living cells and cells
       nuclei
IN     Segev, David, Mazkeret Batia, ISRAEL
PA     Segev Laboratories Limited, Nes Ziona, ISRAEL (non-U.S. corporation)
PI     US 20080004234      A1  20080103
AI     US 2007-806609      A1  20070601 (11)
RLI    Continuation-in-part of Ser. No. US 2005-320411, filed on 29 Dec 2005,
       PENDING Continuation-in-part of Ser. No. WO 2005-US24443, filed on 6 Jul
       2005, PENDING
PRAI   US 2004-585075P     20040706 (60)
       US 2006-809827P     20060601 (60)
DT     Utility
FS     APPLICATION
LREP   Martin D. Moynihan, PRTSI, Inc., P.O. Box 16446, Arlington, VA, 22215,
       US
CLMN   Number of Claims: 54
ECL    Exemplary Claim: 1
DRWN   15 Drawing Page(s)
LN.CNT 5291
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     A novel class of oligomeric compounds designed for forming conjugates
       with biologically active substances and delivering these substances to a
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desired bodily target are disclosed. Novel conjugates of these oligomeric compounds and biologically active moieties, pharmaceutical compositions containing such conjugates, and uses thereof as delivery systems for delivering the biologically active substances to a desired target are further disclosed. Processes of preparing the conjugates and the oligomeric compounds and novel intermediates designed for and used in these processes are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 6 USPATFULL on STN
AN 2006:189323 USPATFULL
TI System for delivering therapeutic agents into living cells and cells nuclei
IN Segev, David, Mazkeret Batia, ISRAEL
PI US 20060160763 A1 20060720
AI US 2005-320411 A1 20051229 (11)
RLI Continuation-in-part of Ser. No. WO 2005-US24443, filed on 6 Jul 2005, PENDING
PRAI US 2004-585075P 20040706 (60)
DT Utility
FS APPLICATION
LREP Martin D. Moynihan, PRTSI, Inc., P.O. Box 16446, Arlington, VA, 22215, US
CLMN Number of Claims: 77
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 4451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel class of oligomeric compounds designed for forming conjugates with biologically active substances and delivering these substances to a desired bodily target are disclosed. Novel conjugates of these oligomeric compounds and biologically active moieties, pharmaceutical compositions containing such conjugates, and uses thereof as delivery systems for delivering the biologically active substances to a desired target are further disclosed. Processes of preparing the conjugates and the oligomeric compounds and novel intermediates designed for and used in these processes are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 6 USPATFULL on STN
AN 2006:144862 USPATFULL
TI Method of manufacturing labelled oligonucleotide conjugates
IN Stengele, Klaus Peter, Pleiskirchen, GERMANY, FEDERAL REPUBLIC OF
Kvassiouk, Evgueni, Waldkraiburg, GERMANY, FEDERAL REPUBLIC OF
PI US 20060122382 A1 20060608
AI US 2003-531292 A1 20031014 (10)
WO 2003-EP11354 20031014
20051121 PCT 371 date
PRAI DE 2002-10247790 20021014
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201, US
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 487
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method for the manufacture of labeled oligonucleotide conjugates comprising the reaction of (a) an oligonucleotide having a labile protecting group bound to a terminal hydroxy group, and (b) a labeling compound, wherein said labile protecting group is partially or completely substituted by said labeling compound in a nucleophilic substitution reaction. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 6 USPATFULL on STN
AN 2003:295043 USPATFULL
TI Labeled oligonucleotides, methods for making same, and compounds useful therefor
IN Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
Guzaev, Andrei P., Carlsbad, CA, UNITED STATES
PI US 20030208061 A1 20031106
US 6825338 B2 20041130
AI US 2001-823031 A1 20010330 (9)
DT Utility
FS APPLICATION
LREP WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE - 46TH FLOOR, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 60
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 2660
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Selectively functionalized oligonucleotides, methods for making same, and compounds useful therefor are disclosed. The oligonucleotides can be selectively functionalized with a first conjugate group at the 3'-terminial position and optionally functionalized with a second conjugate group at the 5'-terminal position and/or one or more internucleotides. Alternatively, the oligonucleotides can be selectively functionalized with a first conjugate group at the 5'-terminal position and optionally functionalized with a second conjugate group at one or more internucleotides. In yet another embodiment, the oligonucleotides can be functionalized with a first conjugate group at one or more internucleotides and with a second conjugate group at one or more different internucleotides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 6 USPATFULL on STN
AN 2003:258639 USPATFULL
TI 207 human secreted proteins
IN Ni, Jian, Germantown, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
LaFleur, David W., Washington, DC, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Rosen, Craig A., Laytonsville, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Soppet, Daniel R., Centreville, VA, UNITED STATES
Young, Paul E., Gaithersburg, MD, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Florence, Kimberly A., Rockville, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Florence, Charles, Rockville, MD, UNITED STATES
Hu, Jing-Shan, Mountain View, CA, UNITED STATES

Li, Yi, Sunnyvale, CA, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES
Fischer, Carrie L., Burke, VA, UNITED STATES
Ferrie, Ann M., Painted Post, NY, UNITED STATES
Fan, Ping, Potomac, MD, UNITED STATES
Feng, Ping, Gaithersburg, MD, UNITED STATES
Endress, Gregory A., Florence, MA, UNITED STATES
Dillon, Patrick J., Carlsbad, CA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
Brewer, Laurie A., St. Paul, MN, UNITED STATES
Yu, Guo-Liang, Berkeley, CA, UNITED STATES
Zeng, Zhizhen, Lansdale, PA, UNITED STATES
Greene, John M., Gaithersburg, MD, UNITED STATES
PI US 20030181692 A1 20030925
AI US 2001-933767 A1 20010822 (9)
RLI Continuation-in-part of Ser. No. WO 2001-US5614, filed on 21 Feb 2001, PENDING Continuation-in-part of Ser. No. US 1998-205258, filed on 4 Dec 1998, PENDING
PRAI US 2000-184836P 20000224 (60)
US 2000-193170P 20000329 (60)
US 1997-48885P 19970606 (60)
US 1997-49375P 19970606 (60)
US 1997-48881P 19970606 (60)
US 1997-48880P 19970606 (60)
US 1997-48896P 19970606 (60)
US 1997-49020P 19970606 (60)
US 1997-48876P 19970606 (60)
US 1997-48895P 19970606 (60)
US 1997-48884P 19970606 (60)
US 1997-48894P 19970606 (60)
US 1997-48971P 19970606 (60)
US 1997-48964P 19970606 (60)
US 1997-48882P 19970606 (60)
US 1997-48899P 19970606 (60)
US 1997-48893P 19970606 (60)
US 1997-48900P 19970606 (60)
US 1997-48901P 19970606 (60)
US 1997-48892P 19970606 (60)
US 1997-48915P 19970606 (60)
US 1997-49019P 19970606 (60)
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US 1997-49373P 19970606 (60)
US 1997-48875P 19970606 (60)
US 1997-49374P 19970606 (60)
US 1997-48917P 19970606 (60)
US 1997-48949P 19970606 (60)
US 1997-48974P 19970606 (60)
US 1997-48883P 19970606 (60)
US 1997-48897P 19970606 (60)
US 1997-48898P 19970606 (60)
US 1997-48962P 19970606 (60)
US 1997-48963P 19970606 (60)
US 1997-48877P 19970606 (60)
US 1997-48878P 19970606 (60)
US 1997-57645P 19970905 (60)
US 1997-57642P 19970905 (60)
US 1997-57668P 19970905 (60)
US 1997-57635P 19970905 (60)
US 1997-57627P 19970905 (60)

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US 1997-57643P 19970905 (60)
US 1997-57769P 19970905 (60)
US 1997-57763P 19970905 (60)
US 1997-57650P 19970905 (60)
US 1997-57584P 19970905 (60)
US 1997-57647P 19970905 (60)
US 1997-57661P 19970905 (60)
US 1997-57662P 19970905 (60)
US 1997-57646P 19970905 (60)
US 1997-57654P 19970905 (60)
US 1997-57651P 19970905 (60)
US 1997-57644P 19970905 (60)
US 1997-57765P 19970905 (60)
US 1997-57762P 19970905 (60)
US 1997-57775P 19970905 (60)
US 1997-57648P 19970905 (60)
US 1997-57774P 19970905 (60)
US 1997-57649P 19970905 (60)
US 1997-57770P 19970905 (60)
US 1997-57771P 19970905 (60)
US 1997-57761P 19970905 (60)
US 1997-57760P 19970905 (60)
US 1997-57776P 19970905 (60)
US 1997-57778P 19970905 (60)
US 1997-57629P 19970905 (60)
US 1997-57628P 19970905 (60)
US 1997-57777P 19970905 (60)
US 1997-57634P 19970905 (60)
US 1997-70923P 19971218 (60)
US 1998-92921P 19980715 (60)
US 1998-94657P 19980730 (60)
US 1997-70923P 19971218 (60)
US 1998-92921P 19980715 (60)
US 1998-94657P 19980730 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 32746
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 6 USPATFULL on STN
AN 2003:152714 USPATFULL
TI Compositions and methods for labeling oligonucleotides
IN Chiarello, Ronald H., Castro Valley, CA, UNITED STATES
Liu, Wing-Cheong, Belmont, CA, UNITED STATES
Alvarado, Gabriel G., San Mateo, CA, UNITED STATES

PA Syngen, Inc. (U.S. corporation)
PI US 20030104380 A1 20030605
US 20040234957 A9 20041125
US 7183405 B2 20070227
AI US 2001-894423 A1 20010628 (9)
DT Utility
FS APPLICATION
LREP MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA, 94105
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 677
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel method for the labeling of oligonucleotides which results in the economical synthesis of 5' labeled molecules. A set of suitably protected and carefully selected set of amino linkers, a modified deprotination/cleavage protocol and standard coupling methodologies to are used to allow for the convergent synthesis of any number of labeled oligonucleotides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l5 4 kwic

L5 ANSWER 4 OF 6 USPATFULL on STN
SUMM . . . a fluorescent signal is observed. Such a phenomenon has been used to detect formation of a complex between a suitably labeled oligonucleotide and a complementary target nucleic acid. When the oligonucleotide is uncomplexed, the donor and the acceptor groups are sufficiently close. . .
DETD [0126] a) providing a derivatized solid support for oligonucleotide synthesis, said derivatized solid support being derivatized with a group having one of the structures: ##STR13##
DETD [0200] As will be appreciated, one or more of the 2'-, 3'-, and/or 5'-positions of the oligonucleotide comprises a hydroxyl protecting group. A wide variety of hydroxyl protecting groups can be employed in the methods of the invention. Preferably, the protecting group. . .
DETD . . . protecting groups may be performed in a variety of suitable solvents. These solvents include those known to be suitable for protecting group removal in oligonucleotide synthesis. In the case of ammonia, water is the preferred solvent, whereas when using carbonates, alcohols are preferred. Methanol is. . .
DETD . . . 48 h at 55° C. removed 2-(4-methoxybenzamido)ethyl protection to give 46 which contained the second phosphorothioate group for the conjugation. Compound 46 was next labeled with 44 and 47-49 to give a bis-pyrenyl labeled 50 and unsymmetrically labeled 51-53 (Scheme 7 and Table 4). The. . .
DETD . . . treated with ammonium hydroxide for 2 days at RT to give 55 where only the 3'-teminal phosphorothioate group was deprotected. Compound 55 was next labeled with 49. The product was isolated by HPLC, and 2-(4-methoxybenzamido)ethyl protection was removed with concentrated ammonium hydroxide for 48 h. . .
CLM What is claimed is:
. . . of said X and one of said R.sub.2 comprise a conjugate group; comprising the steps of: a) providing a derivatized solid support for oligonucleotide synthesis, said

derivatized solid support being derivatized with a group having one of the structures: ##STR57## wherein T is a bifunctional linking moiety linked to. . .

CLM What is claimed is:

. . . least one of said R.sub.2 or said X comprise a conjugate group; comprising the steps of: a) providing a derivatized solid support for oligonucleotide synthesis, said derivatized solid support being derivatized with a group having one of the structures: ##STR66## wherein T is a bifunctional linking moiety linked to. . .

CLM What is claimed is:

. . . L.sub.1, L.sub.2 and each of said L.sub.3 are, independently, a conjugate group; comprising the steps of: a) providing a derivatized solid support for oligonucleotide synthesis, said derivatized solid support being derivatized with a group having one of the structures: ##STR75## wherein T is a bifunctional linking moiety linked to. . .

CLM What is claimed is:

. . . L.sub.1, L.sub.2 and each of said L.sub.3 are, independently, a conjugate group; comprising the steps of: a) providing, a derivatized solid support for oligonucleotide synthesis, said derivatized solid support being derivatized with a group having one of the structures: ##STR80## wherein T is a bifunctional linking moiety linked to. . .

=> d l5 6 kwic

L5 ANSWER 6 OF 6 USPATFULL on STN

SUMM . . . a suitably protected linker arm phosphoramidite is attached via standard DNA synthesis procedures. Following cleavage and deprotection of the modified oligonucleotide, the label is added to the linker arm in a solution phase reaction. Typically this is accomplished via coupling of an activated. . .

SUMM [0008] In one embodiment, the present invention contemplates a method of labeling oligonucleotides, comprising: a) providing: i) a solid support-bound oligonucleotide comprising an amino group, ii) a bifunctional linker arm and iii) an activated label; b) reacting said solid support-bound oligonucleotide with said bifunctional linker arm to produce a support-bound linker-oligonucleotide, and; c) reacting said support-bound linker-oligonucleotide with said activated label to produce a labeled support-bound oligonucleotide. The present invention also contemplates that the bifunctional linker arm is selected from a group consisting of the compounds listed. . .

SUMM [0009] In another embodiment, the present invention contemplates a method of labeling oligonucleotides, comprising: a) providing: i) a solid support-bound oligonucleotide comprising an amino group, ii) a bifunctional linker arm and iii) an activated label; b) reacting said solid support -bound oligonucleotide with said bifunctional linker arm to produce a support-bound protected linker-oligonucleotide; c) deprotecting the amino group of said support-bound protected linker-oligonucleotide to produce a support-bound deprotected linker-oligonucleotide, and; d) reacting said support-bound deprotected linker-oligonucleotide with said activated label to produce a labeled support-bound protected oligonucleotide. The present invention also contemplates that the bifunctional linker arm is selected from a group consisting of the compounds listed. . .

SUMM . . . hydroxyl group of an oligonucleotide and the second functional group is suitable for coupling with an available functionality on the label compound.

DRWD [0043] FIG. 3 shows one embodiment for the production of a tetramethylrhodamine-labeled oligonucleotide as practiced in the present invention.

DRWD [0044] FIG. 4 shows one embodiment for the synthesis of an amino labeled oligonucleotide as practiced in the present invention.

DRWD [0045] FIG. 5 shows one embodiment for the synthesis of a hydroxyl labeled oligonucleotide as practiced in the present invention.

DETD . . . cation form. Proton donation from the carboxylic acid moiety to the N,N-diisopropylamino could occur and result in reagent instability, compromising oligonucleotide labeling efficiency.

DETD [0049] Some fluorescent dye labels (e.g., fluorescein and related derivatives) retain their fluorescent properties during cleavage of the labeled oligonucleotide from the solid phase support and removal of protecting groups with concentrated aqueous ammonia, the standard method in current practice.. . .

DETD . . . oligonucleotide synthesis techniques. This process is exemplified in FIGS. 1A and 1B, which shows the synthesis of a tetramethylrhodamine (TMR) labeled oligonucleotide.

DETD . . . bifunctional linker arm, in this case N-methylaminoethanol. Such a linker arm serves several functions. It provides needed distance between the label and the oligonucleotide, a functional group, in this case an amine; appropriate for reaction with the tetramethylrhodamine and a functional group, in this. . .

DETD . . . case, rhodamine phosphoramidite is substituted for the nucleoside phosphoramidite and coupled as usual for DNA synthesis. Following oxidation, the support-bound labeled oligonucleotide is cleaved from the support and fully deprotected to yield the final product

DETD . . . is not available. This approach is exemplified in FIGS. 2A and 2B, which illustrate the approach using TMR as the labeling compound. While ultimately producing the same product as the TMR Phosphoramidite, this approach segregates the process into two distinct coupling processes.. . .

DETD . . . the 5' hydroxyl of a support-bound fully protected oligonucleotide via standard DNA synthesis procedures. Following the removal of the amino protecting group, the oligonucleotide is cleaved from the solid supports and deprotected yielding a linker-modified oligonucleotide. This product is then reacted in solution with activated label to yield labeled oligonucleotide.

DETD [0056] Preparation of a TMR-labeled oligonucleotide as practiced in the current invention is detailed in FIG. 3. Conceptually, the approach consists of a novel and empirically. . .

DETD . . . a large variety of labeled oligonucleotides. On a molar basis, the combined cost of the linker phosphoramidite and the basic labeling compound ranges from 10-30% of the cost of a fully prepared label phosphoramidite. In practice, further cost reductions are realized when. . . material would have a useful life less than one week. Use of a common linker phosphoramidite with a variety of labeling compound would greatly reduce such waste in a typical production environment.

DETD . . . hydroxyl group of the oligonucleotide and the second functional group is suitable for coupling with an available functionality on the label compound. If required for chemical compatibility, the second functional group may bear a removable protecting group. After removal any protecting groups, the second

functional groups is then coupled with a labeling compound to produced a labeled oligonucleotide . While it is preferred in some situations to use a carboxyl containing label and a linker that consist of a. . .

DETD . . . with succinic anhydride to provide a carboxy functional group which, in turn, was reacted with the amino group on a labeling compound (FIG. 4).

CLM What is claimed is:

1. A method of labeling oligonucleotides, comprising: a) providing: i) a solid support-bound oligonucleotide comprising an amino group, ii) a bifunctional linker arm and iii) an activated label; b) reacting said solid support -bound oligonucleotide with said bifunctional linker arm to produce a support-bound, linker-oligonucleotide; c) reacting said support-bound linker-oligonucleotide with said activated label to produce a labeled support-bound protected oligonucleotide.

CLM What is claimed is:

4. A method of labeling oligonucleotides, comprising: a) providing: i) a solid support-bound oligonucleotide comprising an amino group, ii) a bifunctional linker arm and iii) an activated label; b) reacting said solid support -bound oligonucleotide with said bifunctional linker arm to produce a support-bound, protected linker-oligonucleotide; c) deprotecting the amino group of said support-bound, protected linker-oligonucleotide to produce a support-bound deprotected linker-oligonucleotide, and; d) reacting said support-bound deprotected linker-oligonucleotide with said activated label to produce a labeled support-bound protected oligonucleotide.